(FILE 'HOME' ENTERED AT 12:08:43 ON 18 JUL 2003)

FILE 'BIOSIS, MEDLINE, CAPLUS' ENTERED AT 12:09:35 ON 18 JUL 2003

L1 8 S (PHOSPHODIESTERASE 1C OR PHOSPHODIESTERASE-1C OR PDE 1C OR PD

L2 5555 S ISOBUTYLMETHYLXANTHIN? OR ZAPRINAST

L3 2 S L1 AND L2

L4 2 DUP REM L3 (0 DUPLICATES REMOVED)

L5 2 S L4 AND PY<19990205

L6 6 DUP REM L1 (2 DUPLICATES REMOVED)

L7 16 S (PHOSPHODIESTERASE 1C OR PHOSPHODIESTERASE-1C OR PDE 1C OR PD

L8 0 S L7 AND (INSULIN SECRET? OR INSULIN? OR BETA-CELL? OR BETA CE

L9 561 S (PHOSPHODIESTERASE 1C OR PHOSPHODIESTERASE-1C OR PDE 1C OR PD

L10 372 S (PHOSPHODIESTERASE 1C OR PHOSPHODIESTERASE-1C OR PDE 1C OR PD

L11 0 S (PHOSPHODIESTERASE 1C OR PHOSPHODIESTERASE-1C OR PDE 1C OR PD

L12 560 S (ZAPRINAST OR ISOBUTYLMETHYLXANTHIN?) AND (BLOOD SUGAR? OR SU

L13 277 DUP REM L12 (283 DUPLICATES REMOVED)

L14 215 S L13 AND PY<1999

L15 2 S L14 AND (ORAL? OR OS OR PERORAL?)

L16 2 DUP REM L15 (0 DUPLICATES REMOVED)

L17 162 S (ZAPRINAST OR ISOBUTYLMETHYLXANTHIN?) AND (BLOOD SUGAR? OR SU

L18 86 DUP REM L17 (76 DUPLICATES REMOVED)

L19 63 S L18 AND PY<1999

WEST Search History

DATE: Friday, July 18, 2003

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ		
L12	(8-methyoxymethyl$17 and xanthine) or (8MM$1IBMX)	1	L12
L11	l3 same oral$2	3	L11
L10	L9 near5 inhibitor	4	L10
L9	PDE1C or PDEIC	14	L9
L8	zaprinast.ti.	3	L8
L7	L3 and (beta$1cell or pancreatic beta cell or pancreatic)	9	L7
L6	L3 and (diabetes or diabeticc or mellitus)	46	L6
L5	L3 and l1	1	L5
L4	L3 same insulin	3	L4
L3	zaprinast	139	L3
L2	phosphodiesterase near9 1C	3	L2
L1	phosphodiesterase 1C	3	L1

END OF SEARCH HISTORY

TITLE: Stimulation of renin secretion by nitric oxide is mediated by **phosphodiesterase** 3.
AUTHOR(S): Kurtz, Armin (1); Goetz, Karl-Heinz; Hamann, Marlies; Wagner, Charlotte
CORPORATE SOURCE: (1) Inst. Physiologie der Univ. Regensburg, D-93040 Regensburg Germany
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (April 14, 1998) Vol. 95, No. 8, pp. 4743-4747.
ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
AB This study aimed to characterize the cellular pathways along which nitric oxide (NO) stimulates renin secretion from the kidney. Using the isolated perfused rat kidney model we found that renin secretion stimulated 4- to 8-fold by low perfusion pressure (40 mmHg), by macula densa inhibition (100 mumol/liter of bumetanide), and by adenylate cyclase activation (3. nmol/liter of isoproterenol) was markedly attenuated by the NO synthase inhibitor nitro-L-arginine methyl ester (L-Name) (1 mM) and that the inhibition by L-Name was compensated by the NO-donor sodium nitroprusside (SNP) (10 mumol/liter). Similarly, inhibition of cAMP degradation by blockade of **phosphodiesterase** 1 (PDE-1) (20 mumol/liter of **8-methoxymethyl**-1-methyl-3-(**2-methylpropyl**)**xanthine**) or of PDE-4 (20 mumol/liter of rolipram) caused a 3- to 4-fold stimulation of renin secretion that was attenuated by L-Name and that was even overcompensated by sodium nitroprusside. Inhibition of PDE-3 by 20 mumol/liter of milrinone or by 200 nmol/liter of trequinsin caused a 5- to 6-fold stimulation of renin secretion that was slightly enhanced by NO synthase inhibition and moderately attenuated by NO donation. Because PDE-3 is a cGMP-inhibited cAMP-PDE the role of endogenous cGMP for the effects of NO was examined by the use of the specific guanylate cyclase inhibitor 1-H(1,2,4)oxodiazolo(4,3a)quinoxalin-1-one (20 mumol). In the presence of 1H-(1,2,4)oxodiazolo(4,3-alpha)quinoxalin-1-one the effect of NO on renin secretion was abolished, whereas PDE-3 inhibitors exerted their normal effects. These findings suggest that PDE-3 plays a major role for the cAMP control of renin secretion. Our findings are compatible with the idea that the stimulatory effects of endogenous and exogenous NO on renin secretion are mediated by a cGMP-induced inhibition of cAMP degradation.

L7 ANSWER 5 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 5
ACCESSION NUMBER: 1998:128545 BIOSIS
DOCUMENT NUMBER: PREV199800128545
TITLE: Effect of selective **phosphodiesterase** inhibitors on response of ovine pulmonary arteries to prostaglandin E2.
AUTHOR(S): Gao, Yuansheng (1); Tolsa, Jean-Francois; Shen, Hai; Usha-Raj, J.
CORPORATE SOURCE: (1) Harbor-UCLA Med. Cent., Res. Education Inst., 1124 W. Carson St., RB-1, Torrance, CA 90502 USA
SOURCE: Journal of Applied Physiology, (Jan., 1998) Vol. 84, No. 1, pp. 13-18.
ISSN: 8750-7587.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Several adenosine 3',5'-cyclic monophosphate (cAMP)-hydrolyzing **phosphodiesterase** isozymes are present in the pulmonary vasculature. The present study was designed to determine the effect of selective inhibitors of **phosphodiesterase** subtypes on prostaglandin E2 (PGE2)-induced relaxation of isolated fourth-generation pulmonary arteries of newborn lambs. PGE2 and forskolin caused pulmonary

arteries to relax and induced an increase in the intracellular cAMP content in the vessels. The relaxation and change in cAMP content were augmented by milrinone and rolipram, inhibitors of **phosphodiesterase** type 3 (PDE3) and type 4 (PDE4), respectively. The augmentation in relaxation and the increase in cAMP content caused by milrinone plus rolipram was greater than the sum of the responses caused by either of the inhibitors alone. **8-Methoxymethyl-1-methyl-3-(2-methylpropyl)xanthine**, an inhibitor of **phosphodiesterase** type 1, had no effect on relaxation and change in cAMP induced by PGE2 and forskolin. Acetylcholine alone had no effect on cAMP content in the vessels but augmented the relaxation and the increase in cAMP induced by PGE2 and forskolin in arteries with endothelium. This effect was not observed in arteries without endothelium or in arteries with endothelium treated with NG-nitro-L-arginine. These results suggest that PDE3 and PDE4 are the primary enzymes hydrolyzing cAMP of pulmonary arteries of newborn lambs and that an inhibition of both PDE3 and PDE4 would result in a greater effect than that caused by inhibition of either one of the subtype isozymes alone. Furthermore, endothelium-derived nitric oxide may enhance cAMP-mediated relaxation by inhibition of PDE3.

L7 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1997:186908 BIOSIS
DOCUMENT NUMBER: PREV199799486111
TITLE: Effect of selective **phosphodiesterase** inhibitors on responses of pulmonary arteries of newborn lambs to prostaglandin E-2.
AUTHOR(S): Gao, Y.; Tolsa, J.-F.; Shen, H.; Raj, J. U.
CORPORATE SOURCE: Dep. Pediatrics, Harbor-UCLA Med. Cent., Torrance, CA 90509 USA
SOURCE: FASEB Journal, (1997) Vol. 11, No. 3, pp. A557.
Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology 97 New Orleans, Louisiana, USA April 6-9, 1997
ISSN: 0892-6638.
DOCUMENT TYPE: Conference; Abstract
LANGUAGE: English

L7 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 6
ACCESSION NUMBER: 1997:356683 BIOSIS
DOCUMENT NUMBER: PREV199799663086
TITLE: Modulation of the megakaryoblastic Dami cell line differentiation by **phosphodiesterase** inhibitors and imidazo(1,2-a)pyrazine derivatives.
AUTHOR(S): Zurbonsen, Katja (1); Michel, Alain; Vittet, Daniel; Bonnet, Pierre-Antoine; Chevillard, Claude
CORPORATE SOURCE: (1) INSERM U.300, Fac. Pharmacy, 15, av. Charles Flahaut, F-34060 Montpellier Cedex 2 France
SOURCE: Pharmacology & Toxicology, (1997) Vol. 80, No. 6, pp. 286-289.
ISSN: 0901-9928.
DOCUMENT TYPE: Article
LANGUAGE: English
AB **Phosphodiesterase** inhibitors have been shown to modulate cell differentiation. We have previously shown that a series of imidazo(1,2-a)pyrazine derivatives displayed inhibitory effects on **phosphodiesterase** isoenzymes types III, IV and V isolated from Dami cells and on Dami cell growth. In the present study we have investigated the effect of these derivatives on the expression of two differentiation markers, glycoproteins Ib and IIb/IIIa of the human megakaryoblastic leukaemic Dami cell line in comparison to those elicited

by 3-isobutyl-1-methylxanthine and selective **phosphodiesterase** inhibitors of types I (**8-methoxymethyl**-1-methyl-3-(**2-methylpropyl**) **xanthine**), III (Milrinone), IV (RO-201724) and V (Zaprinast). Imidazo(1,2-a)pyrazine derivatives, 3-isobutyl-1-methylxanthine and selective **phosphodiesterase** inhibitors, except **8-methoxymethyl**-1-methyl-3-(**2-methylpropyl**) **xanthine**, decreased glycoprotein Ib expression. SCA40, SCA41, SCA44 and 3-isobutyl-1-methylxanthine but not the other compounds affected the expression of glycoprotein IIb/IIIa in a positive manner. The effects of imidazo(1,2-a)pyrazine derivatives on glycoprotein expression appeared to be related to their **phosphodiesterase** inhibitory potency.